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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/798,096

03/11/2004

Rea-Min Chu

P/741-176

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10/10/2006

OSTROLENK FABER GERB & SOFFEN

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EXAMINER

BERTOGLIO, VALARIE E

ART UNIT

PAPER NUMBER

1632

DATE MAILED: 10/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/798,096

Applicant(s)

CHU ET AL.

Examiner

Valarie Bertoglio

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02/21/2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 17-22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 17-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>02/21/2006</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The instant application has been transferred to Examiner Valarie Bertoglio, Ph.D., Group Art Unit 1632.

Applicant's reply to the Notice of Non-compliant Amendment filed 07/25/2006 has been received. While the newly submitted claims of 02/21/2006 are not drawn to the elected invention, SEQ ID NO:3 was previously searched and considered in the office action dated 08/26/2005 and therefore it is not considered an undue burden to examine the newly submitted claims 17-27. Therefore, claims 1-16 are cancelled and newly added claims 17-27 are under consideration in the instant office action. .

Specification

The substitute specification submitted 02/21/2006 has been entered. All references to the specification will be with respect to the amended version.

Claim Objections

The objections to the claims are withdrawn in light of Applicant's cancellation of the claims.

Claim 22 is objected to because of the following informalities: The word "and" at line 3 is not consistent with the grammatical format of the claim and should be removed. It also appears the term "wherein" should be inserted at line 5 between the words "IL -15, " and "the plasmid". The claim also recites that the plasmid "is a pcDNA3.1/V5-His-TOPO vector" rather the plasmid "comprises" a pcDNA3.1/V5-His-TOPO" vector backbone. While it is clear what Applicant is intending to claim, the phrase "a pcDNA3.1/V5-His-TOPO vector" could be interpreted to exclude the other limitations of the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112-1st paragraph

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Newly added claims 17-27 are rejected for reasons of record applied to previously pending claims 1-14 and 16 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a therapeutic composition for inhibiting tumor cells producing TGF- β , comprising a plasmid comprising SEQ ID NO:1 encoding IL-6 and a plasmid comprising SEQ ID NO:4 encoding IL-15 operably linked to an IL-2 signal peptide, and a method of inhibiting the growth of the TGF- β producing tumor cells by administering the plasmids via muscle electroporation, does not reasonably provide enablement for a therapeutic composition comprising a plasmid comprising SEQ ID NO:1 encoding IL-6 and a plasmid comprising SEQ ID NO:2 encoding IL-15 without an IL-2 secretion signal sequence, or a method of inhibiting the growth of any tumor cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Applicant's arguments have been considered and are found partially persuasive. The rejection is maintained in part for reason set forth below.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the

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quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The claims are drawn to a composition for gene therapy, comprising a plasmid comprising SEQ ID NO:1, encoding IL-6 and a plasmid encoding SEQ ID NO:3, encoding IL-15, used for treating tumor cells such as CTVT, wherein the composition antagonizes TGF- β and activates NK cells to inhibit the growth of tumor cells, and a method for gene therapy, comprising inhibiting tumor cell growth, such as CTVT with said composition.

The specification provides guidance on the manufacture of two plasmids: one comprising a sequence encoding human IL-6 (SEQ ID NO:1); and the second comprising a sequence encoding human IL-15 operably linked to the human IL-2 signal peptide (SEQ ID NO:4; specification, pg. 13, pgph 40). No other plasmids are disclosed as a therapeutic composition. Further, the specification teaches that when the plasmids are electroporated into CB-17 mice, seven days after the mice were injected with xenogeneic CTVT tumors, the tumors showed a decrease in tumor size at day 14 in comparison to mock controls. Based on these *in vivo* results applicant's claim their instant invention.

1) The aspect of the rejection regarding the breadth of tumors encompassed by the claims is withdrawn. Applicant has narrowed the scope of the claim to tumors producing TGF- β . The specification demonstrates that the claimed therapy is effected through a mechanism involving over-riding the TGF- β signal that is crucial in the growth of tumors that produce TGF- β .

2) Applicant has argued a second aspect of the enablement rejection regarding the plasmids used in the claimed invention. Previously, claim 1 recited use of IL -15 whereas the specification taught use if IL-15 operably linked to a signal sequence from IL2. The newly added claims recite SEQ ID NO:3, which

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encodes IL -15 alone, and does not include the IL2 signal peptide, which is present in the plasmid used in the instant invention. While the specification fails to explain the purpose of the signal peptide, a review of the literature demonstrates that an IL2SP/IL15 fusion protein is secreted as a result of the presence of the IL2SP. The instant invention appears to necessitate the secretion of IL15 for its function. Applicant's arguments (page 8 of Applicant's Remarks dated 02/21/2006) appear to pertain to the breadth of the plasmid backbone which is not subject to this rejection. Therefore, this aspect of the rejection is maintained.

3) The third aspect of the rejection addressed by Applicant is regarding the method of delivery of the plasmid in the claimed method (claims 22-27). Claim 22 has been limited to electroporation of the muscle and thus, this aspect of the rejection is withdrawn.

4) The fourth aspect of the rejection addressed by applicant is regarding the possibility that the claimed treatment is acting directly on the tumor cells or through macrophage activation as opposed to NK cells as described in the specification. Applicant's remarks are persuasive as set forth at pages 8 (bottom)-11 (top). This aspect of the rejection is withdrawn.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claim 4 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of Applicant's cancellation of the claim.

Claims 22-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 is incomplete as written. The preamble of the claim is drawn to a method of inhibiting

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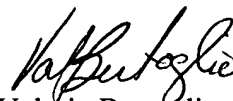
Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Valarie Bertoglio
Examiner
Art Unit 1632